



PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Use as many sheets as necessary)</i>				Application Number	10/590,445 - Conf. # 6734
				Filing Date	August 24, 2006
				First Named Inventor	Michael Jung
				Art Unit	1614
				Examiner Name	James D. Anderson
Sheet	1	of	7	Attorney Docket Number	58086-235854

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No.	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
	A1	4,097,578	06-27-1978	Perronnet et al.	
	A2	4,399,216	08-16-1983	Axel et al.	
	A3	4,559,157	12-17-1985	Smith et al.	
	A4	4,608,392	08-26-1986	Jacquet et al.	
	A5	4,820,508	04-11-1989	Wortzman	
	A6	4,938,949	07-03-1990	Borch et al.	
	A7	4,992,478	02-12-1991	Geria	
	A8	5,010,182	04-23-1991	Brake et al.	
	A9	5,411,981	05-02-1995	Gaillard-Kelly et al.	
	A10	5,434,176	07-18-1995	Claussner et al.	
	A11	5,705,654	01-06-1998	Claussner et al.	
	A12	5,985,868	11-16-1999	Gray	
	A13	6,087,509	07-11-2000	Claussner et al.	
	A14	6,479,063	11-12-2002	Weisman et al.	
	A15	6,489,163	12-03-2002	Roy et al.	
	A16	6,506,607	01-14-2003	Shyjan	
	A17	2004/0009969	01-15-2004	Cleve et al.	
	A18	2002/0133833 A1	09-19-2002	Sawyers et al.	
	A19	6,828,471	12-07-04	Sawyers et al.	

Examiner Signature	/Savitha Rao/	Date Considered	07/16/2008
--------------------	---------------	-----------------	------------

PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		Application Number	10/590,445 - Conf. # 6734
		Filing Date	August 24, 2006
		First Named Inventor	Michael Jung
		Art Unit	1614
		Examiner Name	James D. Anderson
Sheet	2	of	7
		Attorney Docket Number	58086-235854

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No.	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Country Code <sup>2</sup> Number <sup>3</sup> Kind Code <sup>4</sup> (if known)			
	B1	EP 362,179	04-04-1990	Smithkline Beecham Corporation	
	B2	WO 00/17103 (with English abstract)	03-08-2000	Yamanouchi Pharmaceutical Co., Ltd., et al.	
	B2	WO 00/43646 (with English abstract)	11-15-2000	Transgene S.A., Achatetier, et al.	
	B4	WO 97/00071	01-03-1997	Biophysica Foundation Sovak, et al.	
	B5	WO 2006/124118	11-23-2006	The Regents of the University of California	
	B6	WO 2005/060661	07-07-2005	The Regents of the University of California	
	B7	WO 2005/059109	06-30-2005	The Regents of the University of California	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kind's Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language translation is attached.

NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No.	Include name of the author ( in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
	C1	Wallen et al., "Androgen Receptor Gene Mutations in Hormone-Refractory Prostate Cancer", J. Pathology 1999, Vol. 189, pages 559-563.			
	C2	Lu et al. "Molecular Mechanisms of Androgen-Independent Growth of Human Prostate Cancer LNCaP-AI Cells", Endocrinology 1999, Vol. 140, No. 11, pages 5054-5059.			
	C2	<del>Karp et al., Cancer Res. 59: 5547-5556.</del>			
	C4	Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).			
	C5	Sambrook et al., Molecular Cloning: A Laboratory Manual 2 <sup>nd</sup> edition (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.			
	C6	Chang et al., Science 240 (4850), 324-326 (1988).			
	C7	NM_000044< <a href="http://www.ncbi.nlm.nih.gov:80/entrez/viewer.fcgi?cmd=Retrieve&amp;db=nucleotide&amp;list_uids=21322251&amp;dopt=GenBank&amp;term=sapiens+AR+androgen+receptor+prostate+cancer&amp;qty=1&gt;gi:21322251">http://www.ncbi.nlm.nih.gov:80/entrez/viewer.fcgi?cmd=Retrieve&amp;db=nucleotide&amp;list_uids=21322251&amp;dopt=GenBank&amp;term=sapiens+AR+androgen+receptor+prostate+cancer&amp;qty=1&gt;gi:21322251</a> , printed October 24, 2007.			
	C8	Mammalian Cell Biotechnology: a Practical Approach. M. Butler, ed. (IRL Press, 1991).			
	C9	Graham and van der Eb, Virology, 52: 450-467.			

Examiner Signature	/Savitha Rao/	Date Considered	07/16/2008
-----------------------	---------------	--------------------	------------

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Number	10/590,445 – Conf. # 6734
Filing Date	August 24, 2006
First Named Inventor	Michael Jung
Art Unit	1614
Examiner Name	James D. Anderson
Attorney Docket Number	58086-235854

Examiner Signature	/Savitha Rao/	Date Considered	07/16/2008
-----------------------	---------------	--------------------	------------

PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO		<b>Complete if Known</b>			
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		Application Number	10/590,445 - Conf. # 6734		
		Filing Date	August 24, 2006		
		First Named Inventor	Michael Jung		
		Art Unit	1614		
		Examiner Name	James D. Anderson		
Sheet	4	of	7	Attorney Docket Number	58086-235854

C32	Gregory, C.W. et al. A mechanism for androgen receptor-mediated prostate cancer recurrence after androgen deprivation therapy. <i>Cancer Res</i> 61, 4315-9 (2001).	
C33	Li, P. et al. Heterogeneous expression and functions of androgen receptor co-factors in primary prostate cancer. <i>Am J Pathol</i> 161, 1467-74 (2002).	
C34	Glass, C.K. & Rosenfeld, M.G. The coregulator exchange in transcriptional functions of nuclear receptors. <i>Genes Dev</i> 14, 121-41 (2000).	
C35	Raffo, A.J. et al. Overexpression of bcl-2 protects prostate cancer cells from apoptosis in vitro and confers resistance to androgen depletion in vivo. <i>Cancer Res</i> 55, 4438-45 (1995).	
C36	McDonnell, T.J. et al. Expression of the protooncogene bcl-2 in the prostate and its association with emergence of androgen-independent prostate cancer. <i>Cancer Res</i> 52, 6940-4 (1992).	
C37	Kinoshita, H. et al. Methylation of the androgen receptor minimal promoter silences transcription in human prostate cancer. <i>Cancer Res</i> 60, 3623-30 (2000).	
C38	Shang, Y., Myers, M. & Brown, M. Formation of the androgen receptor transcription complex. <i>Mol Cell</i> 9, 601-10 (2002).	
C39	Zhau, H.Y. et al. Androgen-repressed phenotype in human prostate cancer. <i>Proc Natl Acad Sci U S A</i> 93, 15152-7 (1996).	
C40	Wainstein, M.A. et al. CWR22: androgen-dependent xenograft model derived from a primary human prostatic carcinoma. <i>Cancer Res</i> 54, 6049-52 (1994).	
C41	Ellis, W.J. et al. Characterization of a novel androgen-sensitive, prostate-specific antigen-producing prostatic carcinoma xenograft: LuCaP 23. <i>Clin Cancer Res</i> 2, 1039-48 (1996).	
C42	Horoszewicz, J.S. et al. LNCaP model of human prostatic carcinoma. <i>Cancer Res</i> 43, 1809-18 (1983).	
C43	Klein, K.A. et al. Progression of metastatic human prostate cancer to androgen independence in immunodeficient SCID mice. <i>Nat Med</i> 3, 402-8 (1997).	
C44	Perou, C.M. et al. Molecular portraits of human breast tumors. <i>Nature</i> 406, 747-52 (2000).	
C45	Gregory, C.W., Johnson, R.T., Jr., Mohler, J.L., French, F.S. & Wilson, E.M. Androgen receptor stabilization in recurrent prostate cancer is associated with hypersensitivity to low androgen. <i>Cancer Res</i> 61, 2892-8. (2001).	
C46	Huang, Z.Q., Li, J. & Wong, J. AR possess an intrinsic hormone-independent transcriptional activity. <i>Mol Endocrinol</i> 16, 924-37 (2002).	
C47	Matias, P.M. et al. Structural evidence for ligand specificity in the binding domain of the human androgen receptor. Implications for pathogenic gene mutations. <i>J Biol Chem</i> 275, 26164-71 (2000).	
C48	Lobaccaro, J.M. et al. Molecular modeling and in vitro investigations of the human androgen receptor DNA-binding domain: application for the study of two mutations. <i>Mol Cell Endocrinol</i> 116, 137-47 (1996).	
C49	Migliaccio, A. et al. Steroid-induced androgen receptor-oestradiol receptor beta-Src complex triggers prostate cancer cell proliferation. <i>Embo J</i> 19, 5406-17 (2000).	

Examiner Signature	/Savitha Rao/	Date Considered	07/16/2008
--------------------	---------------	-----------------	------------

PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO		<b>Complete if Known</b>			
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		Application Number	10/590,445 - Conf. # 6734		
		Filing Date	August 24, 2006		
		First Named Inventor	Michael Jung		
		Art Unit	1614		
		Examiner Name	James D. Anderson		
Sheet	5	of	7	Attorney Docket Number	58086-235854

C50	Kousteni, S. et al. Nongenotropic, sex-nonspecific signaling through the estrogen or androgen receptors: dissociation from transcriptional activity. Cell 104, 719-30 (2001).	
C51	Manolagas, S.C., Kousteni, S. & Jilka, R.L. Sex steroids and bone. Recent Prog Horm Res 57, 385-409 (2002).	
C52	DePrimo, S.E. et al. Transcriptional programs activated by exposure of human prostate cancer cells to androgen. Genome Biol 3, RESEARCH0032 (2002).	
C53	Masiello, D., Cheng, S., Bubley, G.J., Lu, M.L. & Balk, S.P. Bicalutamide functions as an androgen receptor antagonist by assembly of a transcriptionally inactive receptor. J Biol Chem 277, 26321-6 (2002).	
C54	Edwards, J., Krishna, N.S., Grigor, K.M. & Bartlett, J.M. Androgen receptor gene amplification and protein expression in hormone refractory prostate cancer. Br J Cancer 89, 552-6 (2003).	
C55	Laitinen, S., Karhu, R., Sawyers, C.L., Vessella, R.L. & Visakorpi, T. Chromosomal aberrations in prostate cancer xenografts detected by comparative genomic hybridization. Genes Chromosomes Cancer 35, 66-73 (2002).	
C56	Grad, J.M., Dai, J.L., Wu, S. & Burnstein, K.L. Multiple androgen response elements and a Myc consensus site in the androgen receptor (AR) coding region are involved in androgen-mediated up-regulation of AR messenger RNA. Mol Endocrinol 13, 1896-911 (1999).	
C57	Craft, N. et al. Evidence for clonal outgrowth of androgen-independent prostate cancer cells from androgen-dependent tumors through a two-step process. Cancer Res 59, 5030-6 (1999).	
C58	Ellwood-Yen, K. et al. Myc-driven murine prostate cancer shares molecular features with human prostate tumors. Cancer Cell 4, 223-38 (2003).	
C59	Wang, S. et al. Prostate-specific deletion of the murine Pten tumor suppressor gene leads to metastatic prostate cancer. Cancer Cell 4, 209-21 (2003).	
C60	Shiau, A.K. et al. The structural basis of estrogen receptor/coactivator recognition and the antagonism of this interaction by tamoxifen. Cell 95, 927-37 (1998).	
C61	Norris, J.D. et al. Peptide antagonists of the human estrogen receptor. Science 285, 744-6 (1999).	
C62	Baek, S.H. et al. Exchange of N-CoR corepressor and Tip60 coactivator complexes links gene expression by NF-kappaB and beta-amyloid precursor protein. Cell 110, 55-67 (2002).	
C63	Shang, Y. & Brown, M. Molecular determinants for the tissue specificity of SERMs. Science 295, 2465-8 (2002).	
C64	Schellhammer, P.F. et al. Prostate specific antigen decreases after withdrawal of antiandrogen therapy with bicalutamide or flutamide in patients receiving combined androgen blockade. J Urol 157, 1731-5 (1997).	
C65	Sack, J.S. et al. Crystallographic structures of the ligand-binding domains of the androgen receptor and its T877A mutant complexed with the natural agonist dihydrotestosterone. Proc Natl Acad Sci U S A 98, 4904-9 (2001).	

Examiner Signature	/Savitha Rao/	Date Considered	07/16/2008
--------------------	---------------	-----------------	------------

PTO/SB/08A/B (09-06)  
Approved for use through 03/31/2007, OMB 0651-0031  
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				Application Number	10/590,445 - Conf. # 6734
				Filing Date	August 24, 2006
				First Named Inventor	Michael Jung
				Art Unit	1614
				Examiner Name	James D. Anderson
Sheet	6	of	7	Attorney Docket Number	58086-235854

C66	Zhou, Z.X., Sar, M., Simental, J.A., Lane, M.V. & Wilson, E.M. A ligand-dependent bipartite nuclear targeting signal in the human androgen receptor. Requirement for the DNA-binding domain and modulation by NH2-terminal and carboxyl-terminal sequences. <i>J Biol Chem</i> 269, 13115-23 (1994).	
C67	Chen, C.D., Welsbie, D.S., Tran, C., Baek, S.H., Chen, R., Vessella, R., Rosenfeld, M.G., and Sawyers, C.L., Molecular determinants of resistance to antiandrogen therapy. <i>Nat. Med.</i> , 10: 33-39, 2004.	
C68	<i>The Pharmacological Basis of Therapeutics</i> , Goodman and Gilman, eds., Macmillan Publishing Co., New York.	
C69	<i>The Practice of Medicinal Chemistry</i> , Camille G. Wermuth et al., Ch 31, (Academic Press, 1996).	
C70	<i>Design of Prodrugs</i> , edited by H. Bundgaard, (Elsevier, 1985).	
C71	<i>A Textbook of Drug Design and Development</i> , P. Krogsgaard-Larson and H. Bundgaard, eds. Ch 5, pgs 113-191 (Harwood Academic Publishers, 1991).	
C72	Remington: <i>The Science and Practice of Pharmacy</i> , 19 <sup>th</sup> Edition, Gennaro (ed.) 1995, Mack Publishing Company, Easton, PA.	
C73	Teutsch, G.; Goubet, F.; Battmann, T.; Bonfils, A.; Bouchoux, F.; Ceredo, E.; Goffo, D.; Gaillard-Kelly, M.; Philibert, D. <i>J. Steroid Biochem. Molec. Biol.</i> 1994, 48, 111-119.	
C74	Van Dort, M. E.; Robins, D. M.; Wayburn, B. <i>J. Med. Chem.</i> 2000, 43, 3344-3347.	
C75	Homma, S., et al., "Differential levels of human leukocyte antigen-class I, multidrug-resistance 1 and androgen receptor expressions in untreated prostate cancer cells: the robustness of prostate cancer", <i>Oncol. Rep.</i> 18 (2), 343-346 (2007).	
C76	Cai, C., et al., "c-Jun has multiple enhancing activities in the novel cross talk between the androgen receptor and Ets variant gene 1 in prostate cancer", <i>Mol. Cancer Res.</i> 5 (7), 725-735 (2007).	
C77	Su, Q.R., et al., "Polymorphisms of androgen receptor gene in childhood and adolescent males with first-onset major depressive disorder and association with related symptomatology", <i>Int. J. Neurosci.</i> 117 (7), 903-917 (2007).	
C78	Brockschmidt, F.F., et al., "The two most common alleles of the coding GGN repeat in the androgen receptor gene cause differences in protein function", <i>J. Mol. Endocrinol.</i> 39 (1), 1-8 (2007).	
C79	Hamilton-Reeves, J.M., et al, "Isoflavone-rich soy protein isolate suppresses androgen receptor expression without altering estrogen receptor-beta expression or serum hormonal profiles in men at high risk of prostate cancer", <i>J. Nutr.</i> 137 (7), 1769-1775 (2007).	
C80	Sweet, C.R., et al., "A unique point mutation in the androgen receptor gene in a family with complete androgen insensitivity syndrome", <i>Fertil. Steril.</i> 58 (4), 703-707 (1992).	
C81	Batch, J.A., et al., "Androgen receptor gene mutations identified by SSCP in fourteen subjects with androgen insensitivity syndrome", <i>Hum. Mol. Genet.</i> 1 (7), 497-503 (1992).	

Examiner Signature	/Saviha Rao/	Date Considered	07/16/2008
--------------------	--------------	-----------------	------------

PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				Application Number	10/590,445 - Conf. # 6734
				Filing Date	August 24, 2006
				First Named Inventor	Michael Jung
				Art Unit	1614
				Examiner Name	James D. Anderson
Sheet	7	of	7	Attorney Docket Number	58086-235854

	C82	Wooster, R., et al., "A germline mutation in the androgen receptor gene in two brothers with breast cancer and Reifenshein syndrome", Nat. Genet. 2 (2), 132-134 (1992).	
	C83	Saunders, P.T., et al., "Point mutations detected in the androgen receptor gene of three men with partial androgen insensitivity syndrome", Clin. Endocrinol. (Oxf) 37 (3), 214-220 (1992).	
	C84	Zoppi, S., et al., "Amino acid substitutions in the DNA-binding domain of the human androgen receptor are a frequent cause of receptor-binding positive androgen resistance", Mol. Endocrinol. 6 (3), 409-415 (1992).	
	C85	International Search Report issued in PCT Application PCT/US2006/011417, mailed on July 3, 2006	
	C86	International Search Report issued in PCT Application PCT/US2006/042221, mailed on June 20, 2006	
	C87	Wang, Long G., et al., "Overexpressed androgen receptor linked to p21WAF1 silencing may be responsible for androgen independence and resistance to apoptosis of a prostate cancer cell line", Cancer Research 61 (20), pp. 7544-7551 (October 15, 2001).	
	C88	Shi, Xu-Bao, et al., "Functional analysis of 44 mutant androgen receptors from human prostate cancer", Cancer Research 62 (5), pp. 1496-1502 (March 1, 2002).	
	C89	Navone, N. M., et al., "Model Systems of Prostate Cancer: Uses and Limitations" Cancer Metastasis, Kluwer Academic Publishers, Dordrecht, NL, 17 (4), 1999, pp. 361-371.	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

\*Applicant's unique citation designation number (optional). \*Applicant is to place a check mark here if English language Translation is attached.

Examiner Signature	/Savitha Rao/	Date Considered	07/16/2008
--------------------	---------------	-----------------	------------